Docket No. 826.1335C/WFH

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Kensaku IMAI et al.

Serial No.: Not Yet Assigned

Group Art Unit:

Filed: Concurrently Herewith

Examiner:

For: METHOD AND APPARATUS FOR AUTOMATICALLY REMOVING VECTOR UNIT IN DNA BASE SEQUENCE

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Before examination of the above-identified application, please amend the application as follows:

I. AMENDMENTS

A. In the Claims

Please **CANCEL** claim 1 without prejudice or disclaimer.

Please **ADD** new claims 45-63 as follows:

45. A method for manipulating base sequence data of a vector, comprising:

storing data of a restriction enzyme and data of a base sequence of a restriction enzyme site of a plurality of vectors in a database;

searching for base sequence data of a recombinant DNA obtained by integrating an object DNA fragment into a vector;

obtaining base sequence data of a front restriction enzyme site and base sequence data of a back restriction enzyme site, specified by a restriction enzyme used for cleaving the vector and a restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a first forward retrieval key based on the obtained base sequence data of the front restriction enzyme site and a first backward retrieval key based on the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by the search based on the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment; and

removing the vector at the specified junction.

46. The method according to Claim 45,

wherein sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein, if the restriction enzyme used to cleave the vector and the restriction enzyme used to obtain the object DNA fragment are designated, data of a forward base sequence from a cleaving point in the restriction enzyme site in the multiple cloning site of the

vector are acquired from the database, and a second forward retrieval key is generated based on the acquired forward base sequence data of the cleaving point of the restriction enzyme site of the vector,

performing first homology retrieval on condition that a first similarity value between the retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys is equal to or larger than a predetermined value,

obtaining a candidate for a base sequence at a junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction, screened by using the first retrieval keys, and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

47. The method according to Claim 45,

wherein the sequence data of the first forward retrieval key and of the first backward retrieval key are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme site in the multiple cloning site,

wherein, if the restriction enzyme used to cleave the vector and the restriction enzyme used to obtain the object DNA fragment are designated, forward base sequence data of

a forward cleaving point of the restriction enzyme site of the vector, and backward base sequence data of a backward cleaving point of the vector are acquired from the database, and a second forward retrieval key and a second backward retrieval key are generated based on the base sequence data of the acquired forward and backward base sequence data of the cleaving points, respectively,

performing a first homology retrieval on condition that a first similarity value between the retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys are equal to or larger than a predetermined value,

obtaining a candidate for a base sequence at a junction between the vector and the object DNA fragment according to a result of the first homology retrieval, and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a plurality of first candidates for the junction, screened by using the first retrieval keys, and base sequence data of the second forward retrieval key, is equal to or larger than a predetermined value.

48. The method according to Claim 47, wherein the sequence data of the first forward and first backward retrieval keys are generated by base sequence data of the vector entered in a vector database, data of a multiple cloning site in the vector, and data of a restriction enzyme size in the multiple cloning site, and

wherein the second homology retrieval is performed using both the second

forward and second backward retrieval keys.

49. The method according to Claim 47,

wherein, if the restriction enzyme used to cleave the vector and the restriction enzyme used to obtain the object DNA fragment are designated, base sequence data of an area before the cleaved portion in the multiple cloning site of the vector corresponding to the designated restriction enzyme are acquired from the database, and a second forward retrieval key is generated based on the acquired base sequence data of the area before the cleaved portion, and

wherein a second homology retrieval is performed on condition that a second similarity value between base sequence data of a first candidate of a junction narrowed by a retrieval using the retrieval key and base sequence data of the second forward retrieval key is equal to or larger than a predetermined value.

50. The method according to Claim 45,

wherein, if the restriction enzyme used to cleave the vector and a restriction enzyme used to obtain the object DNA fragment are designated, backward base sequence data from a cleaving point in a multiple cloning site of the vector corresponding to the designated restriction enzyme are acquired from the database, and a second backward retrieval key is generated based on the acquired backward base sequence data of the cleaving point, and

performing a first homology retrieval on condition that a first similarity value between the retrieval base sequence data of the recombinant DNA and the first forward and first backward retrieval keys are equal to or larger than a predetermined value;

obtaining a candidate for a base sequence at a junction between the vector and the object DNA fragment according to a result of the first homology retrieval; and

performing a second homology retrieval on condition that a second similarity value between base sequence data of a first candidate for the junction, screened by using the first retrieval keys, and base sequence data of the second backward retrieval key is equal to or larger than a predetermined value.

51. The method according to Claim 50,

wherein said vector is removed from the recombinant DNA sequence data, when the area specified by the second homology retrieval is one.

52. The method according to Claim 47, further comprising:

obtaining, as a forward vector unit candidate for the vector base sequence, a forward base sequence specified as a result of the second homology retrieval and a base sequence before said forward base sequence; and

obtaining, as a backward vector unit candidate for the vector base sequence, a backward base sequence specified as a result of the second homology retrieval and a base

sequence after said backward base sequence.

53. The method according to Claim 51,

wherein said forward vector unit candidate and said backward vector unit candidate are removed from the recombinant DNA sequence data, when there is only one candidate respectively for the specified forward and backward vector units, and the specified forward and backward vector units do not overlap each other.

54. A device for removing a vector from a recombinant DNA base sequence, obtained as a result of performing a cloning process by integrating an object DNA fragment into a vector, comprising:

a database storing data of a restriction enzyme, and data of base sequences of a restriction enzyme site of a plurality of vectors;

an obtaining unit obtaining base sequence data of a front restriction enzyme site and base sequence data of a back restriction enzyme site, specified by the restriction enzyme used for cleaving the vector and the restriction enzyme used for obtaining the object DNA fragment, from the database;

a generation unit generating a first forward retrieval key based on the obtained base sequence data of the front restriction enzyme site of a vector, and a first backward retrieval key based on the base sequence data of the back restriction enzyme site; and

a retrieving unit retrieving base sequence data of the recombinant DNA obtained based on the first forward and first backward retrieval keys, and specifying a junction between the vector and the object DNA fragment based on the retrieval result.

55. The device according to Claim 54, further comprising:

display means,

wherein said vector is included in a vector list displayed on said display means, and

wherein at least one of said specified restriction enzymes is included in a restriction enzyme list displayed on said display means.

56. The device according to Claim 54, further comprising:

program storage means for storing at least one of:

a program for generating the retrieval keys by controlling said generation unit;

a program for specifying the vector base sequence by controlling said retrieving unit; and

a program for removing the vector base sequence.

57. The device according to Claim 54,

wherein said retrieving unit specifies using the first retrieval key as a junction

between the vector base sequence data and the object DNA fragment sequence data.

58. The device according to Claim 57,

wherein said retrieving unit specifies, as the junction, a portion in the DNA base sequence data in which a number of bases matching a base sequence of the first retrieval key is equal to or larger than a predetermined value.

59. The device according to Claim 54,

wherein said retrieving unit specifies using, as the first retrieval key, a first junction and a second junction between the vector base sequence and the object DNA fragment.

60. The device according to Claim 54,

wherein said retrieval key is first forward and first backward retrieval keys including sequence data including an end portion of the object DNA fragment and sequence data including an end portion of the vector base sequence, and specifies a candidate for a junction between the vector base sequence and the object DNA fragment.

61. The device according to Claim 60,

wherein a second retrieval key, including sequence data longer than that of said

first forward and first backward retrieval keys, is generated, and the junction is specified using the second retrieval key.

62. The device according to Claim 61,

wherein said object DNA fragment is specified by removing the junction and sequence data distal to the junction and the object DNA fragment from the DNA base sequence.

63. A computer-readable storage medium on which is recorded a program enabling a computer to execute an operation process of a base sequence of a recombinant DNA obtained by integrating an object DNA into a vector, said process comprising the steps of:

storing data of a restriction enzyme and data of a base sequence of a restriction enzyme site of a plurality of vectors in a database;

obtaining base sequence data, of a front restriction enzyme site and base sequence data of a back restriction enzyme site, specified by the restriction enzyme used for cleaving the vector and the restriction enzyme used for obtaining the object DNA fragment, from the database;

generating a forward retrieval key based on the obtained base sequence data of the front restriction enzyme site, and a backward retrieval key based on the obtained base sequence data of the back restriction enzyme site;

retrieving base sequence data of the recombinant DNA obtained by a search based on the forward and backward retrieval keys, and

specifying a junction between the vector and the object DNA fragment for removing the vector.

REMARKS

A. The August 18, 2000 Office Action

In the Office Action, pending claims 23-26, 28, 29, 31-34 and 36-44 were rejected under 35 U.S.C. §§ 102, 103 and 112. These claims are canceled, and new claims 45-63 are added corresponding thereto.

B. Rejection of Claims Under 35 U.S.C. §§102/103

In the last Response, Applicant amended the independent claims to recite details about determining the first forward and backward retrieval keys using base sequence data of respective restriction enzymes.

Nevertheless, so amended claims 23, 34, 36-41 and 44 were rejected again as being anticipated by Smith et al., and so amended claims 24-26, 28, 29, 31-33, 42 and 43 were rejected as being made obvious by this reference, citing page 1015 thereof, which states:

> Prior to assembly, the raw sequences can be checked for the presence of a vector sequence that could adversely affect the assembly. The vector sequences

> can be manually entered or imported from a file...The user then establishes the percentage of bases in the cloning vector sequence that must match the bases at the head or at the tail of a fragment sequence to designate a cloning vector. Sequence regions matching the cloning vector at, or above, the specified percentage are automatically removed from the sequence.

Based on this quote, the Examiner concludes that "Smith et al. describe a ... method for removing vector sequences from DNA sequence data by a process of identifying known vector sequences at the beginning and the end of the insert sequence of interest in the DNA sequence data and removing the identified vector sequences...restriction enzyme site detection and storage...is inherent in detection and storage of vector sequences because the vector sequences designated to be deleted comprise restriction enzyme sites." (Emphasis supplied).

In response, it is respectfully submitted that Smith et al. fails to anticipate or render obvious new claims 45-68.

Initially, as noted in the November 12, 1999 Response, "a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular combination." In re Spormann, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966). In the present case, it is respectfully submitted that Smith et al. has been cited for including certain inherent teachings, but there has been no explanation as to why such inherency exists in Smith et al., and why one of ordinary skill would be motivated to

rely upon this inherent teaching (if it exists) to arrive at the present invention.

Further, while the claims include numerous limitations, the Examiner has failed to state with specificity the grounds for finding these limitations anticipated or rendered obvious, which is respectfully believed to be inconsistent with PTO Rule 1.104 and MPEP Sections 707.02j and 707.07.

Due to the above-discussed rejection based on inherency and/or the lack of citation of specific disclosure/teaching in the reference relative to the specific recitations of the claims, it is expressly requested that the Examiner better explain the meaning and scope of the Smith et al. reference "teaching", the source of such understanding, and provide an actual application of the disclosure/teaching of Smith against the claim limitations. Under the circumstances, it is respectfully submitted that a final rejection would not be proper.

Notwithstanding the above, as indicated, the examiner has concluded that restriction enzyme site detection is inherent in Smith et al. because the vector sequences designated to be deleted by Smith et al. necessarily comprise restriction enzyme sites. However, just because vector sequences designated to be deleted comprise restriction enzyme sites does not mean that the invention reciting the use of the enzyme sites to determine when and where to remove the vector is anticipated or made obvious.

Smith et al. does not describe using a search key, the base sequence of the restriction-enzyme site that is determined by the restriction-enzyme. Respectfully, the Examiner does not

provide any reasons such a recitation is anticipated or rendered obvious. Instead the Examiner appears to be rejecting the claims merely on Smith et al.'s general or conceptual terms.

Further, at a minimum, there may be other characteristics of the sequences that are also known, but what is the motivation to rely upon any particular characteristics when seeking to improve upon the quality of the desired, isolated object DNA sequences? Thus, while Smith et al. may have a similar goal to the present invention, there is no enabling teaching as to how to obtain the goal. In any case, any suggestion of the "how to" does not arrive at the present invention.

That is, the above quote of Smith et al., and the remainder of the reference, make no mention of any specific vector, lack any discussion of any retrieval key, restriction enzymes or sequence information about the enzymes, and certainly lack any teaching of forward and backward retrieval keys determined using base sequence data of respective restriction enzymes, as recited in the claims herein.

At most, Smith et al. identifies sequences of a vector that match with the head and the end of the inserted fragment sequence, and that the vector can be deleted by knowing the fragment sequence at the head and the end. Smith et al., however, does not teach, at least, determining the interconnecting plane between a vector and the object DNA fragment by using as a retrieval key, the base sequence of the restriction enzyme site that is specified by the restriction enzyme used for cleaving the vector.

C. Section 112, 2nd Paragraph Rejections

In the Office Action, various terms in the claims were considered unclear.

As the Applicant requests above clarification/elaboration of the prior art rejections, and as those clarifications/elaborations may effect claim amendments, it is respectfully requested that any amendments to address the Section 112, para. 2, rejections be deferred to the response to the first Office Action in this continuation application.

III. CONCLUSION

If there are any remaining formal matters that need to be attended to in this application, it is requested that the Examiner contact the undersigned attorney at the below-identified telephone number at the Examiner's convenience.

If there are any additional fees associated with this Response, please charge same to our Deposit Account No. 19-3935.

Respectfully submitted,

Date: 2/20/01

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